

A Pilot Study Investigating Clinical Responses and Biological Pathways of Azelastine/Fluticasone in Nonallergic Vasomotor Rhinitis before and after Cold Dry Air Provocation.

Abstract

BACKGROUND:

Nonallergic vasomotor rhinitis (NAVMR) has been considered a diagnosis by exclusion due to unknown mechanisms or lack of diagnostic biomarkers.

METHODS:

To determine clinical responses and biological pathways in NAVMR subjects challenged to cold dry air (CDA) in an environmental exposure chamber (EEC) pre- and posttreatment with azelastine/fluticasone (AzeFlu), 30 NAVMR subjects, prescreened for CDA-induced symptoms (approx. 14°C, <15% relative humidity, ×1 h) were randomized to treatment with AzeFlu (n = 20) or placebo (n = 10) for 2 weeks. Total nasal symptoms scores, minimum cross-sectional area, cough, and conjunctival redness were recorded at visit 1 (pretreatment) and visit 2 (posttreatment) before, during, and after CDA challenge. At both visits, nasal lavage fluid (NLF) and nasal scrapings (NS) were collected pre- and post-CDA challenge. Substance P, neurokinin-A, and calcitonin gene-related peptide concentrations in NLF were analyzed pre- and postchallenge at each visit. Their relationship with CDA-induced symptoms was determined by statistical analysis. MicroRNA sequencing from NS determined differentially expressed miRNA between the treatment groups post-CDA challenge at each visit.

RESULTS:

The minimum cross-sectional area ($p < 0.05$), cough count ($p < 0.05$), and substance P ($p < 0.01$) improved posttreatment with AzeFlu versus placebo. Gene targets for differentially expressed miRNAs at visit 1 were enriched for biological pathways regulating epithelial ciliogenesis and cell integrity that were modified in the AzeFlu-treated group versus placebo posttreatment.

CONCLUSIONS:

This study demonstrated the feasibility of an EEC model to investigate CDA-induced clinical responses and pathobiology in NAVMR subjects pre- and posttreatment with AzeFlu. NAVMR disease mechanisms for other nonallergic triggers can be investigated similarly.